UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/804,678	03/19/2004	Saverio Carl Falco	BB1037USCNT	9737

23906 7590 08/22/2008

E I DU PONT DE NEMOURS AND COMPANY
LEGAL PATENT RECORDS CENTER
BARLEY MILL PLAZA 25/1122B
4417 LANCASTER PIKE
WILMINGTON, DE 19805

EXAMINER	
MCELWAIN, ELIZABETH F	

ART UNIT	PAPER NUMBER
1638	

NOTIFICATION DATE	DELIVERY MODE
08/22/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-Legal.PRC@usa.dupont.com

Office Action Summary	Application No.	Applicant(s)	
	10/804,678	FALCO ET AL.	
	Examiner	Art Unit	
	Elizabeth F. McElwain	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Brief filed June 13, 2008 has been entered.

On further consideration of the claims the Final Rejection has been withdrawn and the following Non-Final Office Action is set forth.

Claims 39-53 are pending and are examined on the merits.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 39-53 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to a chimeric gene comprising a nucleic acid sequence encoding all or a part of a plant lysine ketoglutarate reductase/saccharopine dehydrogenase (LKR/SDH) that is sufficient for use in antisense inhibition or sense suppression to cause an increase level of lysine in seeds of a plant transformed with said chimeric gene. In addition, claims 49-53 are drawn to a chimeric gene wherein the LKR/SDH coding sequence comprises all or part of SEQ ID NO: 120 that is sufficient for use in antisense inhibition or sense suppression. However, the specification fails to describe the structural features that are essential for LKR activity. Therefore, it remains unclear what constitutes a nucleic acid sequence encoding an

LKR or part of the same. In addition, the specification discusses that LKR sequences have homology to saccharopine dehydrogenases (SDH), and sometimes LKR and SDH are in a single bi-functional protein (pages 31-36). However, no information is provided regarding what structural features would confer either type of enzyme activity, and furthermore what sequences would be sufficient for use in antisense inhibition or sense suppression of LKR/SDH. The claims are broadly drawn to a genus of sequences, including any nucleic acid fragment that comprises part of a nucleic acid sequence that encodes a plant lysine ketoglutarate reductase/saccharopine dehydrogenase that is useful in antisense inhibition or sense suppression of said LKR/SDH activity and can increase the lysine in seeds. However, the specification does not provide any examples of nucleic acids that have the claimed functional activity, much less a representative number that would provide a written description of the genus claimed.

"A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." In addition, "The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA . . . Accordingly, the specification does not provide a written description of the invention". See *University of California v. Eli Lilly and Co.,* 119 F. 3d 1559; 43 USPQ 2d 1398, 1406 (Fed. Cir. 1997).

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, one skilled in the art would not have been in possession of the genus claimed at the time this application was filed.

3. Applicants' arguments filed June 13, 2008 have been fully considered but they are not persuasive. Applicants assert that Drs. Falco and Epelbaum were the first to report the cloning of a plant LKR/SDH genomic and DNA sequence and this was published subsequent to filing and that their post-filing date publication sets forth a comparison of the deduced amino acid sequences of a plant LKR/SDH with three fungal sequences. The Examiner responds that the specification teaches that several such sequences were known in the prior art (see page 4 of the specification). However, the specification does not disclose or describe any sequences or sequence motifs that are required to confer the functional activity claimed, including any fragments of the undisclosed sequences that may be used for antisense inhibition or sense suppression in order to increase lysine in a plant seed. Applicants' post-filing date publication is does not overcome the absence of information in the specification with regard to structural features that are required to define the claimed genus.

4. Applicants also point to the Declaration of Falco as providing evidence for the use of one nucleic acid fragment of 1268 bp that includes the LKR domain from the corn LKR-SDH sequence of (SEQ ID NO: 120) to increase lysine in a plant. However, the Examiner maintains that the Declaration of Falco does not relate the experimental method and sequences to those set forth in the specification. Furthermore, one example is not sufficient to describe the claimed genus. Applicants also point to other post-filing date publications to support their claims. However, post-filing date publications cannot overcome deficiencies in the specification for written description of the claimed invention.

Claim Rejections - 35 USC § 112

5. Claims 39-53 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are drawn to a chimeric gene comprising a nucleic acid sequence encoding all or a part of a plant lysine ketoglutarate reductase/saccharopine dehydrogenase (LKR/SDH) that is sufficient for use in antisense inhibition or sense suppression to cause an increase level of lysine in seeds of a plant transformed with said chimeric gene. In addition, claims 49-53 are drawn to a chimeric gene wherein the LKR/SDH coding sequence comprises all or part of SEQ ID NO: 120 that is sufficient for use in antisense inhibition or sense suppression. However, the specification does not demonstrate that any of the claimed sequences have homology to saccharopine dehydrogenases (SDH), and sometimes LKR and SDH are in a single bi-functional protein (pages 31-36). In addition, the specification discloses that SEQ ID NO: 120 and 122 are not full length sequences (page 34). Therefore, it is even more uncertain that the claimed sequences would encode the portions required to confer LKR activity.

It is well established that sequence homology is not sufficient to predict function of encoded sequences. See the teachings of Doerks (TIG 14, no. 6: 248-250, June 1998), where it states that computer analysis of genome sequences is flawed, and "overpredictions are common because the highest scoring database protein does not necessarily share the same or even similar functions" (the last sentence of the first paragraph of page 248). Doerks also teaches homologs that did not have the same catalytic activity because active site residues were not conserved

(page 248, the first sentence of the last paragraph). In addition, Smith et al (Nature Biotechnology 15:1222-1223, November 1997) teach that "there are numerous cases in which proteins of very different functions are homologous" (page 1222, the first sentence of the last paragraph). Also, Brenner (TIG 15, 4:132-133, April 1999) discusses the problem of inferring function from homology, stating that "most homologs must have different molecular and cellular functions" (see the second full paragraph of the second column of page 132, for example). Furthermore, Borks (TIG 12, 10:425-427, October 1996) teaches numerous problems with the sequence databases that can result in the misinterpretation of sequence data.

In addition, De Luca teaches that modifying plant biosynthetic pathways by transforming plants with genes encoding enzymes involved in a biosynthetic pathway is highly unpredictable (see the paragraph bridging the columns on page 225N, for example), and that "on many occasions desired goals have been impossible to achieve" (see the last paragraph on page 228N). Therefore, both the identification of other genes encoding LKR/SDH activity, and the modification of lysine levels by transforming a plant with said gene or a portion of said gene are highly unpredictable.

Thus, given the unpredictability of identifying sequences that exhibit LKR/SDH activity and modifying the lysine levels of a plant; the lack of guidance in the specification for identifying and characterizing sequences that LKR/SDH activity; the lack of working examples of LKR/SDH coding sequences to modify lysine levels in a plant, and the lack of working examples of similar sequences that encode proteins having the same activity; and the breadth of the claims, and use of said genes to modify lysine levels; it would require undue experimentation by one skilled in the art to make and use the invention as broadly claimed.

6. Applicants' arguments filed June 13, 2008 have been fully considered but they are not persuasive. Applicants argue that the Declaration of Falco of February 16, 2001 demonstrates that an increase in lysine was obtained in seeds obtained from plants co-transformed with DHDPS and LKR and that the LKR sequence is a 1268 bp fragment of obtained from the near full length corn LKR/SDH. The Examiner maintains that the claims are not drawn to co-transformation of a plant with DHDPS and LKR, but to transformation with all or part of LKR/SDH. In addition, the Declaration of Falco does not relate the methods or sequences used to those that are set forth in the specification.

7. In addition, applicants have submitted sequence alignments and state that plant LKR domains share about 70% and 60% sequence identity, and plant SDH domains share about 60% sequence identity with one another, while yeast and plant sequences are less similar. Applicants argue that from these alignments one of skill in the art could identify which amino acids are required for functional activity. The Examiner maintains that the claims are drawn to nucleic acid sequences for use in antisense inhibition and sense suppression, and not to expression of functional enzymes. The Examiner maintains that the specification does not teach what nucleic acid sequence fragments will function to increase lysine in seeds by decreasing expression of LKR/SDH. The Examiner maintains that it would require undue experimentation to make and/or use the invention, for the reasons already of record.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claim 39 is rejected under 35 U.S.C. 102(a or b) as being anticipated by Applicants' admitted state of the prior art.

9. The claim is drawn to a chimeric gene comprising an isolated nucleic acid fragment comprising all or part of a nucleic acid sequence encoding a plant lysine ketoglutarate reductase/saccharopine dehydrogenase and at least one regulatory sequence operably linked to said fragment. The additional limitations in the claim are all drawn to intended use.

10. Applicants' admitted state of the prior art teaches that numerous sequences or partial sequences of LKR/SDH genes were known in the prior art (see page 4 of the specification), wherein the cloning and sequencing of said nucleic acids would require the production of chimeric genes having the nucleic acids operably linked to regulatory sequences. And the ability to increase lysine levels in seeds and the ability to inhibit or suppress expression of the endogenous gene would be an inherent property of the same nucleic acid.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 39-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lundquist et al (US Patent 6,329,574) taken with Applicant's admitted state of the prior art.

14. Lundquist et al teach a high lysine transgenic corn plant having increased lysine levels in the seed (paragraphs 459-469 of the Detailed Description and the claims). Lundquist et al also teach increasing lysine in corn seed by introducing into a corn plant nucleic acid sequences operably linked to regulatory sequences that eliminate expression of genes encoding enzymes in the lysine biosynthesis pathway, such as LKR (see paragraph 125 of the Brief Summary).

15. Lundquist et al do not specifically teach an LKR and/or SDH coding sequence.

16. Applicants' admitted state of the prior art teaches that LKR/SDH coding sequences were known in the prior art, as stated above.

17. Given the recognition of the desirability of producing corn with increased levels of lysine by transforming a corn plant with a chimeric gene that comprises at least part of a nucleic that encodes an enzyme in the lysine biosynthesis pathway, such as LKR, as taught by Lundquist et al, it would have been obvious to one of ordinary skill in the art to make a high lysine corn plant using the methods taught by Lundquist et al and to substitute any of the known LKR coding sequences that were known, as taught by Applicants' admitted state of the prior art, and in view of the suggestion of Lundquist et al to use an LKR coding sequence to reduce gene expression of

LKR in a corn plant in order to increase lysine levels in a corn seed. Thus, the claimed invention would have been prima facie obvious as a whole to one of ordinary skill in the art at the time it was made, especially in the absence of evidence to the contrary.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth F. McElwain whose telephone number is (571) 272-0802. The examiner can normally be reached on increased flex time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

EFM

/Elizabeth F. McElwain/
Primary Examiner, Art Unit 1638